Paper No. 37

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KENNETH WALSH

Appeal No. 2004-1957
Application No. 09/408,905

ON BRIEF

Before WINTERS, SCHEINER and ADAMS, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of claims 1-4. Claim 5 is also pending but stands objected to; claims 6-38 are pending, but have been withdrawn from consideration.

Claim 1 is representative:

1. A method for treating myocardial infarction comprising: administering to a subject in need of such treatment an Akt molecule in an amount effective to inhibit cardiac tissue necrosis in the subject.

The references relied on by the examiner are:

Datta, et al. (Datta), "Akt Phosphorylation of BAD Couples Survival Signals to the Cell-Intrinsic Death Machinery," Cell, Vol. 91, pp. 231-241 (October 17, 1997)

Cuevas et al. (Cuevas), "Fibroblast Growth Factor-1 Prevents Myocardial Apoptosis Triggered by Ischemia Reperfusion Injury," Eur. J. Med. Res., Vol. 2, pp. 465-468 (November 28, 1997)

Claims 1-4 stand rejected under 35 U.S.C. § 103 as unpatentable over Cuevas and Datta.[1] We reverse this rejection.

BACKGROUND

> Programmed cell-death (also known as apoptosis) . . . is a characteristic of the normal developmental process as well as a response of cells to stress or other environmental insults. Apoptosis is characterized by membrane blebbing . . . , cellular and cytoplasmic shrinkage, chromosome fragmentation and condensation, and endonuclease activation . . . Apoptosis does not induce an inflammatory response because cells form apoptotic bodies which are phagocytozed by neighboring cells. A number of stresses can induce apoptosis in vitro and in vivo. The administration of glucocorticoids, reduction of hormone and/or growth factor levels, chemotherapy (toxic agents), mechanical injury and DNA damage can all result in apoptosis. Apoptosis is also induced by aberrant cell cycle activity, and it can be triggered in cells that express the Fas receptor with crosslinking antibodies or the natural Fas ligand. High frequencies of apoptotic cell-death are associated [with] a diverse array of pathological disorders.

Specification, page 1.

"Akt (c-Akt) is a proto-oncogene encoding a serine-threonine kinase . . . It is the cellular homolog of the viral oncoprotein v-Akt, and is related to protein kinase-C (PKC) within the catalytic domain . . . Activation of Akt reportedly inhibits apoptosis induced by growth factor withdrawal or irradiation in neural cells, fibroblasts, and lymphocytes . . . Recently, it has been reported that Akt phosphorylates the pro-apoptotic protein *Bad* leading to *Bad* inactivation and cell survival" (Specification, pages 1-2). "The invention involves the discovery that Akt . . . inhibits apoptotic cell-death of cells, and in particular, inhibits apoptotic cell-death of cardiomyocytes, skeletal myocytes and/or vascular endothelial cells" (id., page 2).

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[1] The Examiner's Answer refers us to Paper No. 13 for the statement of the rejection.

DISCUSSION

The claimed invention is a method of treating myocardial infarction by administering to a subject in need thereof an amount of Akt effective to inhibit cardiac tissue necrosis in the subject (see claim 1).

Cuevas teaches that "[i]schemia-reperfusion-induced myocardial injury is associated with neutrophil accumulation, a burst of oxygen free radical production, calcium overload and apoptosis" (Cuevas, page 465, right-hand column). "Since alterations in calcium homeostasis are involved in apoptosis [ ], and fibroblast growth factor (FGF) prevents apoptosis in differentiated cells [ ]," and "FGF has previously been shown to attenuate neutrophil infiltration in ischemic reperfused myocardium" (id., page 467, left-hand column), Cuevas suggests that FGF-1 (acidic FGF) "could protect cardiac myocytes against myocardial-ischemia-reperfusion injury by normalization of calcium homeostasis [ ] and attenuation of neutrophil infiltration" (id., page 465, right-hand column).

Datta teaches that "Akt is a general mediator of growth-factor induced survival" and "suppress[es] the apoptotic death of a number of cells types induced by a variety of stimuli, including growth factor withdrawal, cell-cycle discordance, loss of cell adhesion, and DNA damage" (Datta, page 231, right-hand column). Through a series of experiments performed in neurons, "a signaling pathway has been defined in which growth factor receptor activation leads to the sequential activation of [phosphatidylinositide-3'-OH kinase] and Akt, which then, through as-yet undescribed mechanisms, promotes cell survival and blocks apoptosis" (id.).

According to the examiner, it would have been obvious to "substitute the apoptotic inhibitor used by Cuevas [ ] with the Akt molecule taught by Datta [ ] in order to treat a myocardial infarction because both molecules are well-known in the art to function as inhibitors of apoptosis" (paper no. 13, page 5). In addition, the examiner argues that "Akt has been shown to suppress the apoptotic death of a number of cell types . . . induced by a variety of stimuli" (Answer, page 4), thus, it would have been reasonable to expect "that Akt would inhibit apoptosis in . . . cardiac myocytes" (id., page 5).

Appellant argues that "neurons and cardiac myocytes are so plainly distinct in their structure and function, one . . . would not expect that a compound that induces apoptosis in one cell type would necessarily have the same effect in another cell type, in the absence of . . . information linking the apoptotic pathways of the cells . . . [nor would one] expect that Akt, an apoptosis inhibitor reported to be effective in neurons, would be effective in cardiac myocytes" (Brief, page 6). Similarly, appellant argues that "[t]he expression of Akt in one cell type would not lead one . . . to have a reasonable expectation that Akt would be expressed in a completely different cell type and in response to different and more complex stimuli, e.g., ischemia and ischemia-reperfusion injury which involves the accumulation of metabolic waste products, changes in mechanical factors and the generation of toxic substances" (id., page 7).

In addition, appellant argues that "apoptosis [ ] is heterogeneous in nature" (Brief, page 8). "[I]n apoptosis there is an 'intrinsic' cell death pathway and an 'extrinsic' cell death pathway[;] [t]he intrinsic pathway functions through the mitochondria and is largely sensitive to Akt[;] [i]n contrast, the extrinsic pathway . . . is largely insensitive to

Akt" (id.). According to appellant, Datta "teaches that Akt-mediated cell survival is mediated by the ability of Akt to phosphorylate and thereby inactivate BAD, a pro-apoptotic protein relevant to the intrinsic cell death pathway," but "[t]here is no teaching or suggestion in either Datta [ ] or Cuevas [ ] that the cell death pathway in myocardial infarction or in ischemia-reperfusion injury involves the intrinsic cell death pathway" (id., pages 8-9). In appellant's view, the references support the opposite conclusion because "(i) Cuevas teaches the beneficial effects of FGF-1, a growth factor known not to act through Akt, and (ii) Datta [ ] teaches that BAD-independent survival mechanisms likely also exist . . . together, [Datta and Cuevas] suggest that FGF-1 and Akt are not interchangeable . . . because FGF-1 may act through a pathway that has no connection to Akt or BAD" (Id., page 9). Finally, appellant argues that "individual growth factors and their receptors" are cell specific and "may invoke different and non-intersecting intracellular signaling pathways . . . [i]t is therefore untenable to suppose that for any given cell type, one apoptosis inhibitor can arbitrarily be substituted for another" (id.).

In our view, neither the examiner's argument nor appellant's response is supported by much in the way of evidence. Nevertheless, "the examiner bears the initial burden of presenting a prima facie case of obviousness." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). The examiner may establish a case of prima facie obviousness based on a combination of references "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992).

Here, the only common ground between Cuevas and Datta "is that each relates, in a general sense, to an apoptotic process" (Brief, page 5). Beyond that, these references, together with the specification (all we have to go on), tend to support appellant's assertion that apoptosis proceeds along many different pathways involving various stimuli, inducers and inhibitors. In our opinion, the mere fact that both FGF and Akt were known to inhibit apoptosis is insufficient basis to establish that one of ordinary skill in the art would have regarded them as interchangeable (or, stated another way, would have regarded Akt as a universal apoptosis inhibitor), given the apparent complexity and variability of the apoptotic process.

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992), citing In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). As set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

> A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. [ ] Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher." [ ]
>
> Most if not all inventions arise from a combination of old elements. [ ] Thus, every element of a claimed invention may often be found in the prior art. [ ] However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. [ ] Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [citations omitted]

In other words, "there still must be evidence that 'a skilled artisan, . . . with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.'" Ecolochem Inc. v. Southern California Edison, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075-76 (Fed. Cir. 2000). The fact that the prior art could have been modified in a manner consistent with appellant's claims would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). On this record, the only reason or suggestion to combine the references in the manner claimed comes from appellant's specification.

Accordingly, the rejection of claims 1-4 under 35 U.S.C. § 103 is reversed.

REVERSED

Sherman D. Winters
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

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